27. (Twice Amended) A dosage form according to claim 1 comprising an inert diluent component is an amount of up to 20% by weight of the dosage form.

REMARKS

Claims 1-38 are pending in this application. By this Amendment, claims 1, 11, 16, 20, 26 and 27 are amended. No new matter is added.

Election/Restriction

In the Examiner's opinion, the claims as currently on file relate to two separate inventions, as set out in paragraph 3 of the official action.

The claims have been amended so that they relate to a single invention. Claim 11 has been amended so that it is now dependent on claim 3 and claim 20 has been amended so that it is dependent on claim 1. In other words, claims 11 and 20 and their dependent claims are now limited to methods and processes for producing the dosage forms of the present invention.

Rejoinder of claims 11-15, 20-25 and 32-37 to the claims of Group I is respectfully requested.

35 U.S.C. 112

The Office Action rejects claims 1 to 10, 16 to 19, 26 to 31 and 38 under 35 U.S.C. § 112, second paragraph for containing asserted informalities. It is in particular

asserted that it is not clear which components of the dosage form of the invention are in homogeneous admixture. To address this point, claims 1, 16 and 25 have been amended to make it clear that all of the listed components of the dosage form are in homogeneous admixture. There is clear basis for this in the specification (see, for example, page 15, lines 10 to 12 and the description of the method used to prepare the tablets of the Examples on page 19).

For at least these reasons, reconsideration and withdrawal of the rejections of claims 1-10, 16-19, 26-31 and 38 under 35 U.S.C. § 112, second paragraph are respectfully requested.

Novelty

The Office Action rejects claims 1, 4 to 10, 27 to 29 and 38 under 35 U.S.C. § 102(b) as being anticipated by the disclosure of US-A-5380535. Applicants traverse this rejection.

Claim 1 is directed to a solid non-effervescent compressed dosage form that is suitable for oral administration and comprises 35% or more by weight of a racemic ibuprofen medicament in homogeneous admixture with a carrier material. The carrier material comprises a compressible filler component combined with a disintegrating component and 3 to 20% by weight of the dosage form of a solid alkali metal carbonate or bicarbonate. The dosage form has a crushing strength of from 6.5 to 15 Kp and a disintegration time of less than 10 minutes and does not contain a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen.

US-A-5380535 relates to a non-aqueous, chewable composition for oral delivery of unpalatable drugs. The compositions described contain a matrix of a drug, such as ibuprofen, and a lipid and comprise one or more solid granulating agents and optionally minor amounts of additives. Suitable additives include buffering agents such as sodium bicarbonate, which may be present in an amount of from about 0.1 to about 20, preferably from about 0.1 to about 10, more preferably from about 1 to about 5 weight percent. The compositions may also comprise a dispersal agent such a starch, cellulose or derivatives thereof, which may be present in an amount of up to 40, generally form about 1 to about 30 percent, preferably from about 2 to about 20, more preferably from about 7 to about 15 weight percent.

The text at column 8, lines 1 to 36 of US-A-5380535 lists suitable amounts of the compounds of the composition when the drug is ibuprofen. For example, such compositions contain 0.1 to 75, preferably 0.5 to 40, most preferably 1 to 25 % by weight of ibuprofen. Suitable amounts of other components of the compositions such as granulating agents (e.g. mannitol), dispersal agents (e.g. hydroxyethyl cellulose, corn starch an croscarmellose sodium), sweeteners and flavouring agents are also given in this section of the text. However, US-A-5380535 contains no suggestion in this section of text that the ibuprofen containing compositions can contain a buffering agent such as sodium bicarbonate. These is also nothing to suggest that this section of the text should be read in combination with that at column 6, lines 16 to 28 relating to the use of sodium bicarbonate. Thus, the text at column 8, lines 1 to 36 of US-A-5380535 does not explicitly disclose a composition comprising all of the components of the dosage forms of the present invention.

The Examiner considers that Examples 3 and 5 and claims 3 and 17 of US-A-5380535 are particularly relevant to the subject matter of the present application.

The composition of Example 3 of US-A-5380535 does not appear to comprise a disintegrating agent as required by claim 1 of the present application.

The composition of Example 5 of US-A-5380535 does not comprise an alkali metal carbonate or bicarbonate, which is an essential component of the dosage forms of claim 1.

Additionally, none of the claims of US-A-5380535 define a composition containing an alkali metal carbonate or bicarbonate.

In other words, none of the sections of US-A-5380535 identified by the Examiner explicitly disclose a dosage form having the combination of components specified in claim 1 of the present application.

In addition, US-A-5380535 is entirely silent as regards the crushing strengths and disintegration times of the compositions it describes. It is essential that the dosage forms of the present invention have a crushing strength and a disintegration time within specified ranges.

In summary, US-A-5380535 does not disclose a dosage form having the combination of features specified in claim 1 of the present application. The subject matter claimed is, therefore, novel over the disclosure of US-A-5380535.

The Office Action has commented that the limitation recited in claims 4, 27 and 30 do not add anything to the claims because the phrase "up to" includes zero as a lower limit. While I agree with his interpretation of this phrase in general, it is respectfully submitted that the comments regarding claims 4 and 30 are incorrect.

Claim 4 is dependent on claim 1 and claim 30 is dependent on claim 3, which is itself dependent on claim 1. Thus, these claims require the limitations of claim 1. According to claim 1, the disintegrating component is an essential feature of the claimed dosage form. Thus, by virtue of their dependency, the dosage forms of claims 4 and 30 cannot contain zero disintegrant.

As regards claim 27, Applicants have amended the wording of this claim so that it is clear that the claimed dosage form must contain some inert diluent component.

For at least the above reasons, reconsideration and withdrawal of the rejections of claims 1, 4-10, 27-29 and 38 under 35 U.S.C. § 102(b) are respectfully requested.

Obviousness

The Office Action asserts that the subject matter of claims 1 to 10, 16 to 19, 26 to 31 and 38 is obvious over the disclosure of US-A-5380535 in light of US-A-4844907. The Office Action also asserts that the subject matter of claims 1 to 10, 27 to 31 and 38 is obvious under 35 U.S.C. § 103(a) in view of the disclosure of US-A-5380535 in the light of US-A-5262179. Applicants traverse these rejections.

The object of the present invention is to provide a solid non-effervescent compressed dosage form which ensures rapid disintegration but also provides a tablet that is both not too large for patient consumption and can be manufactured using standard processes (see page 1, lines 24 to 27). This problem is solved by providing dosage forms as defined in claim 1, which have a crushing strength of form 6.5 to 15 Kp and a disintegrating time of less than 10 minutes.

The objectives of the cited prior art documents are entirely different.

US-A-5380535 is concerned with providing a chewable dosage form that is suitable for patients who have difficulty swallowing tablets. This is achieved by providing a composition in which the pharmaceutically active agent is intimately dispersed or dissolved in a pharmaceutically acceptable lipid.

US-A-4844907 is concerned with overcoming the poor pharmaceutical qualities of known tablets containing a combined of a narcotic analgesic and a non-steroidal anti-inflammatory carboxylic acid such as a combination of codeine and ibuprofen. This problem is solved in US-A-4844907 by providing a table containing the narcotic and the anti-inflammatory agent in separate phases, for example by providing a layered tablet structure.

US-A-5262179 relates to soluble forms of ibuprofen medicaments and addresses the problem of masking the taste of ibuprofen water-soluble salts of ibuprofen. This is achieved by the addition of an alkali metal bicarbonate such as sodium bicarbonate, an alkali metal monohydrogen phosphate or an alkali metal tribasic citrate.

The person of ordinary skill in the art attempting to solve the problem of the present invention would not have even considered the teaching of any of these cited documents, as they are entirely silent on the problem addressed by the present invention.

However, even if one of ordinary skill in the art had considered the teaching of any of the cited documents, alone or in combination, (which it is submitted they would not have) the skilled person would not have arrived at the presently claimed invention.

As discussed above in relation to novelty, US-A05380535 does not explicitly disclose a dosage form having all of the essential components of the dosage form of the

present invention. A large number of potential components that could be included in the compositions of US-A05380535 are described in US-A-5380535. There is nothing in that document that would have encouraged the person of ordinary skill in the art to make the selections necessary to produce a dosage form having the components used in the dosage forms of the present invention in the stated amounts.

There is certainly nothing in US-A-5380535 that would have led the skilled person to expect that a dosage form comprising the specified amounts of each of the components specified in claim 1 would have the advantageous combination of crushing strength and disintegration time achieved by the dosage forms of the presently claimed invention. In fact, US-A-5380535 is entirely silent with respect to crushing strengths and disintegration times. Thus, the skilled person reading US-A-5380535 would not have been taught what crushing strengths and disintegration times are desirable, let alone how to achieve them.

More particularly, there is nothing in US-A-5380535 that would have led the person of ordinary skill in the art to expect that the inclusion of 3 to 20 % by weight of the dosage form of an alkali metal carbonate or bicarbonate in an ibuprofen containing dosage form would have improved the compressibility of the dosage form as found by the present inventors (see page 3, lines 10 to 12 of the present application).

In summary, the teaching of US-A-5380535 would not have encouraged or enabled the person of ordinary skill in the art to produce a dosage form as claimed in the present application.

Even if the person of ordinary skill in the art had also considered the teaching of US-A-4844907, he still would not have arrived at the presently claimed invention.

As discussed above, US-A- 4844907 is concerned with an entirely different problem to that addressed by the present invention. The skilled person reading that document would not have been provided with any teaching that would have suggested how to modify compositions such as those described in US-A-5380535 in order to solve the problems addressed by the present invention.

US-A-4844907 is concerned with improving the pharmaceutical activity of dosage forms comprising both a narcotic analgesic or a salt thereof and a non-steroidal anti-inflammatory carboxylic acid or a salt or ester thereof. There is no mention in US-A-4844907 of the desirability of providing dosage forms having the combination of crushing strength and disintegration time provided by the dosage forms of the presently claimed invention. Thus, the teaching of US-A-4844907 does not add anything to the teaching of US-A-5380535 that would have encouraged or enabled the person of ordinary skill in the art to produce dosage forms as claimed in the present application.

The one thing that US-A-4844907 does teach is that it is possible to produce an ibuprofen containing dosage form having a layered structure. A dosage form having a layered structure is the subject of claim 26 of the present application. In addition to the layered structure, the dosage form of claim 26 has the same features as the dosage form of claim 1. As discussed above it would not have been obvious in view of the teaching of US-A-5380535 and US-A-4844907 to provide a dosage form having all of the features of the dosage form of claim 1. Thus, the disclosure of the dosage form having a layered structure in US-A-4844907 does not render the subject matter of claim 26 obvious.

Likewise, even if the person of ordinary skill in the art had considered the teaching of US-A-5380535 in combination with that of US-A-5262179, he would not have arrived at the presently claimed invention.

US-A-5362179 describes compositions of water-soluble salts of ibuprofen. These compositions comprise an alkali metal bicarbonate, alkali metal monohydrogen phosphate or alkali metal tribasic citrate to mask the taste of the soluble ibuprofen salt. In the presently claimed invention, the alkali metal carbonate or bicarbonate is used for an entirely different purpose. As indicated at page 3, lines 10 to 14 of the present application, the presence of the alkali metal carbonate or bicarbonate enhances the compressibility of the compositions. As a result, solid dosage forms having an advantageous combination of hardness and disintegration characteristics are produced.

The skilled person reading US-A-5262179 would have had no expectation that these advantageous results could be achieved. As illustrated by the Examples of US-A-5262179, the dosage forms described in that document are not even in the form of compressed, solid dosage forms, rather they are in the form of powders that are contained in a sachet. Thus, there is nothing in US-A-5262179 that would have suggested to the person of ordinary skill in the art that an alkali metal carbonate or bicarbonate could have been used to improve the compressibility of an ibuprofen containing compositions. There is certainly nothing in US-A-5262179 that would have taught the skilled person what amount of alkali metal carbonate or bicarbonate would be useful for this purpose.

In summary, the compositions of the present invention would not have been obvious in view of the disclosure of the documents cited in the Office Action. Thus,

reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) of claims 1-10, 16-19, 26-31 and 38 and of 1-10, 27-31 and 38 are respectfully requested.

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300.

Respectfully submitted,

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MARKED-UP AMENDMENTS TO THE CLAIMS

1. (Twice Amended) A solid non-effervescent compressed dosage form suitable for oral administration comprising a racemic ibuprofen medicament present to an extent of 35% or more by weight of the dosage form and in homogeneous admixture with a carrier material comprising

i) a compressible filler component combined with a disintegrating component,

ii) 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form;

[said solid alkali metal carbonate or bicarbonate being in homogeneous admixture with said ibuprogen medicament and said compressible filler component with disintegrating component,]

wherein the dosage form has a crushing strength in the range 6.5-15Kp and a disintegration time of less than 10 minutes,

provided that the ibuprofen medicament does not contain a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen.

11. (Twice Amended) A method of preparing a dosage form according to claim 3 [solid non-effervescent dosage form suitable for oral administration of a solid salt of racemic ibuprofen] comprising the steps of:

mixing a carrier material with the ibuprofen medicament under dry conditions, wherein the carrier material comprises 3-20% alkali metal carbonate or bicarbonate by weight of the dosage form, 10-50% compressible filler component by weight of the

dosage form and up to 15% of a disintegrating component by weight of the dosage form to obtain a mixture and then compressing said mixture [into a solid non-effervescent dosage form having a crushing strength in the range 6.5-15Kp and a disintegration time of less than 10 minutes, wherein the sodium salt of racemic ibuprofen comprises at least 35% by weight of the dosage form].

16. (Twice Amended) A method of obtaining an onset-hastened analgesic and/or anti-pyretic response comprising the oral administration of a non-effervescent compressed solid dosage form comprising 35% or more by weight of a racemic ibuprofen medicament <u>in homogeneous admixture</u> [together] with a carrier material comprising

i) a compressible filler component combined with a disintegrating component, and

ii) 3-20%solid alkali metal carbonate or bicarbonate by weight of the dosage form,

[said solid alkali metal carbonate or bicarbonate being in homogeneous admixture with said ibprofen medicament and said compressible filler component with disintegrating component,]

wherein the dosage form has a crushing strength in the range 6.5-15 Kp and a disintegration time of less than 10 minutes,

provided that the ibuprofen medicament does not include a calcium salt of ibuprofen in combination with an alkali metal salt of ibuprofen.

20. (Twice Amended) A process to prepare a [non-effervescent solid] dosage form according to claim 1, [suitable for oral administration comprising a racemic ibuprofen medicament present to an extent of 35% or more by weight of the dosage form characterized by] which comprises combining a carrier material comprising 8-80% compressible filler component by weight of the carrier 10-20% disintegrating component by weight of the carrier, 8-40% alkali metal carbonate or bicarbonate by weight of the carrier, with 35% or more by eight of the dosage form of the ibuprofen medicament to form a homogeneous solid mixture under dry conditions optionally with other tabletting excipients and compressing the mixture into one or more solid dosage forms [having a crushing strength in the range 6.5-15 Kp and a disintegration time of less than 10 minutes].

26. (Twice Amended) A solid formulation having a layer comprising a composition comprising a racemic ibuprofen medicament in homogeneous admixture [together] with a carrier material, the racemic ibuprofen medicament being present to an extent of 35% or more by weight of the composition and the carrier material comprising a compressible filler component combined with a disintegrating component characterised in that the carrier material comprises 3-20% solid alkali metal carbonate or bicarbonate by weight of the dosage form,

[said solid alkali metal carbonate or bicarbonate being in homogeneous admixture with said ibuprofen medicament and said compressible filler component with disintegrating component,]

wherein the composition is capable of compression to provide a layer having a

crushing strength in the range 6.5-15Kp and a disintegration time of less than 10 minutes.

27. (Twice Amended) A dosage form according to claim 1 comprising [up to 20% by weight of] an inert diluent component is an amount of up to 20% by weight of the dosage form.